



General

Guideline Title

Symptom management in patients with lung cancer: diagnosis and management of lung cancer, 3rd ed: American College of Chest Physicians evidence-based clinical practice guidelines.

Bibliographic Source(s)

Simoff MJ, Lally B, Slade MG, Goldberg WG, Lee P, Michaud GC, Wahidi MM, Chawla M. Symptom management in patients with lung cancer: diagnosis and management of lung cancer, 3rd ed: American College of Chest Physicians evidence-based clinical practice guidelines. Chest. 2013 May;143(5 Suppl):e455S-97S. [295 references] [PubMed](#)

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: Kvale PA, Selecky PA, Prakash UB, American College of Chest Physicians. Palliative care in lung cancer: ACCP evidence-based clinical practice guidelines (2nd edition). Chest. 2007 Sep;132(3 Suppl):368S-403S.

Regulatory Alert

FDA Warning/Regulatory Alert

Note from the National Guideline Clearinghouse: This guideline references a drug(s) for which important revised regulatory and/or warning information has been released.

- [August 31, 2016 – Opioid pain and cough medicines combined with benzodiazepines](#) : A U.S. Food and Drug Administration (FDA) review has found that the growing combined use of opioid medicines with benzodiazepines or other drugs that depress the central nervous system (CNS) has resulted in serious side effects, including slowed or difficult breathing and deaths. FDA is adding Boxed Warnings to the drug labeling of prescription opioid pain and prescription opioid cough medicines and benzodiazepines.
- [March 22, 2016 – Opioid pain medicines](#) : The U.S. Food and Drug Administration (FDA) is warning about several safety issues with the entire class of opioid pain medicines. These safety risks are potentially harmful interactions with numerous other medications, problems with the adrenal glands, and decreased sex hormone levels. They are requiring changes to the labels of all opioid drugs to warn about these risks.

Recommendations

Major Recommendations

The grades of recommendation (1A–2C) and the approach to rating the quality of evidence are defined at the end of the "Major Recommendations" field.

Pain Control

In patients with lung cancer who experience chronic pain, it is suggested that thorough assessment of the patient and his or her pain should be performed (Grade 2C).

Remark: A patient-reported pain scale should be the principal tool to assess their pain.

Remark: Visual analog scales (VASs), numerical rating scales (NRSs) and verbal rating scales are also suggested tools for rating pain.

In patients with lung cancer who experience chronic pain, the use of the World Health Organization (WHO) analgesic ladder to plan treatment is suggested (Grade 2C).

In patients with lung cancer who are being treated at all stages of the WHO analgesic ladder, it is recommended that acetaminophen and/or a non-steroidal anti-inflammatory drug (NSAID) be prescribed unless contraindicated (Grade 1A).

In lung cancer patients with chronic pain who are taking NSAIDs and who are at high risk of gastrointestinal bleeding it is recommended that they take either misoprostol 800 mcg/day, standard dose proton pump inhibitors, or double-dose histamine H2 antagonists (Grade 1A).

In patients with chronic neuropathic pain due to cancer, treatment with an anticonvulsant (e.g., pregabalin, gabapentin, or carbamazepine) or a tricyclic antidepressant (e.g., amitriptyline or imipramine) is recommended (Grade 1A).

In patients with chronic pain due to lung cancer, the use of ketamine, lidocaine 5% plasters, and cannabinoids is not recommended (Grade 1A).

In lung cancer patients with mild to moderate chronic pain (score 3–6 on a VAS or NRS), it is recommended that codeine or dihydrocodeine be added to acetaminophen and/or NSAID (Grade 1C).

In lung cancer patients with severe chronic pain, oral morphine is recommended as first-line treatment (Grade 1C).

In lung cancer patients with severe chronic pain, oxycodone or hydromorphone are recommended as alternatives when there are significant side effects or lack of efficacy with oral morphine (Grade 1A).

In lung cancer patients with severe chronic pain who are able to swallow, transdermal fentanyl is not recommended for first-line use (Grade 1C).

In lung cancer patients with stable, severe, chronic cancer pain who have difficulty swallowing, nausea and vomiting, or other adverse effect from oral medications, transdermal fentanyl is recommended as an alternative to oral morphine (Grade 1B).

In lung cancer patients with severe chronic pain, it is suggested that the prescription of methadone as an alternative to oral morphine be confined to a specialist in palliative care units with experience in methadone prescription, because of difficulties with dose prediction, adjustment, and drug accumulation (Grade 2C).

In lung cancer patients with severe chronic cancer pain, treatment with systemic strong opioids is recommended (Grade 1C).

Remark: The oral route of administration is recommended on the grounds of convenience and cost.

In lung cancer patients with severe chronic cancer pain treated with systemic strong opioids who cannot swallow or who suffer excessive nausea and vomiting, the parenteral, transcutaneous or transmucosal route of administration is recommended (Grade 1C).

In the management of pain in lung cancer patients unable to take oral opioids, it is suggested that the subcutaneous route to administer continuous infusion of strong opioids, is equally effective as the intravenous route (Grade 2C).

In lung cancer patients with severe chronic cancer pain treated with systemic strong opioids, dose titration using either immediate release or sustained release oral morphine is suggested (Grade 2B).

Remark: The recommended starting dose is oral morphine 30 mg/24 h in patients not previously treated with opioids, and 60 mg/24 h in those already taking an opioid at step 2 of the WHO ladder. Where immediate release oral morphine is used, the four-hourly dose is used to treat episodes of uncontrolled pain and in this context may be used up to hourly. The total dose administered in 24 h is used to calculate ongoing opioid requirements. Where sustained release morphine is used, the total estimated daily dose is prescribed as once-daily or twice-daily oral morphine.

In lung cancer patients with severe chronic cancer pain treated with systemic strong opioids who experience breakthrough pain, parenteral

morphine or transmucosal fentanyl citrate are recommended (Grade 1B).

Remark: Oral transmucosal fentanyl citrate (OTFC), fentanyl buccal tablet (FBT), and transnasal fentanyl spray are all effective formulations for breakthrough pain.

Remark: In patients with severe chronic cancer pain who experience a lack of effective analgesia, or uncontrollable side effects, or both, it is appropriate to switch to an alternative strong opioid, or route of administration, or both, though evidence of benefit from this approach is lacking.

Management of Airway Obstruction

In lung cancer patients with inoperable disease and symptomatic airway obstruction, therapeutic bronchoscopy employing mechanical debriement, brachytherapy, tumor ablation, or airway stent placement is recommended for improvement in dyspnea, cough, hemoptysis, and overall quality of life (QOL) (Grade 1C).

Palliation of Cough

In all lung cancer patients with troublesome cough, evaluation for other treatable causes of cough, in addition to cancer-related etiologies is recommended (Grade 1C).

In all lung cancer patients with troublesome cough without a treatable cause, it is recommended that opioids be used to suppress the cough (Grade 1B).

In all lung cancer patients with troublesome cough attributed to chemotherapy or radiation-induced pneumonitis, anti-inflammatory therapy with corticosteroids is recommended (Grade 1C).

Remark: Macrolides can be considered as steroid-sparing agents.

Palliation of Bone Metastasis

In patients with lung cancer who have pain due to bone metastases, external radiation therapy is recommended for pain relief (Grade 1A).

Remark: A single fraction of 8 Gy is equally effective for immediate relief of pain and more cost-effective than higher fractionated doses of external radiation therapy.

In patients with lung cancer who have painful bone metastases, bisphosphonates are recommended in addition to external beam radiation therapy for pain relief (Grade 1A).

In patients with lung cancer who have painful bone metastases to long and/or weight bearing bones and a solitary well-defined lytic lesion circumferentially involving >50% of the cortex and an expected survival >4 weeks with satisfactory health status, surgical fixation is recommended to minimize the potential for a fracture (Grade 1C).

Remark: Intramedullary nailing is the preferred approach, especially for the femur or the humerus.

Remark: Radiotherapy should follow the orthopedic management 2-4 weeks later.

In patients with lung cancer who have vertebral compression fractures causing pain, vertebral augmentation procedures are recommended to reduce pain (Grade 1A).

Palliation of Brain Metastases

In patients with lung cancer who have symptomatic brain metastases, dexamethasone at 16 mg/day is recommended during the course of definitive therapy with a rapid taper as allowed by neurologic symptoms (Grade 1B).

In lung cancer patients with significant brain edema, neurologic symptoms, or large space occupying brain metastasis (>3 cm), surgical resection is recommended if they are surgical candidates (Grade 1B).

In lung cancer patients with 1 to 3 brain metastases, stereotactic radiosurgery (SRS) alone is the recommended initial therapy (Grade 1A).

Remark: With a low burden of disease, the benefit gained by delaying whole brain radiation therapy outweighs the potential risk.

In patients with 5 or more brain metastases, whole brain radiation is the recommended therapy (Grade 1A).

Palliation of Spinal Cord Compression

In patients with lung cancer that have new onset of back pain, sagittal T1-weighted magnetic resonance imaging (MRI) of the entire spine is recommended (Grade 1C).

In patients with lung cancer and epidural spinal cord metastases, who are not symptomatic, prompt treatment with high-dose dexamethasone and radiotherapy is recommended (Grade 1B).

In lung cancer patients with symptomatic radiographically confirmed epidural spinal cord compression (SCC) and good performance status, it is recommended that neurosurgical consultation be sought and, if appropriate, surgery should be performed immediately and followed by radiation therapy (Grade 1B).

Palliation of Superior Vena Cava (SVC) Obstruction

In patients with SVC obstruction from suspected lung cancer, definitive diagnosis by histologic or cytologic methods is recommended before treatment is started (Grade 1C).

In patients with symptomatic SVC obstruction due to small cell lung cancer (SCLC), chemotherapy is recommended (Grade 1C).

In patients with symptomatic SVC obstruction due to non-small cell lung cancer (NSCLC), radiation therapy and/or stent insertion are recommended (Grade 1C).

Remark: When using stenting for the management of SVC obstruction, consideration of necessary anticoagulation as it relates to future management of the patient must be considered.

In patients with SCLC or NSCLC with SVC obstruction who fail to respond to chemotherapy or radiation therapy, vascular stents are recommended (Grade 1C).

Management of Hemoptysis

In all lung cancer patients with large volume hemoptysis, securing the airway with a single-lumen endotracheal tube is recommended. Bronchoscopy is recommended to identify the source of bleeding, followed by endobronchial management options such as argon plasma coagulation, neodymium-doped:yttrium aluminum garnet (Nd:YAG) laser, and electrocautery for visible central airway lesions (Grade 1C).

In all lung cancer patients with non-large volume hemoptysis, bronchoscopy is recommended to identify the source of bleeding. For visible central airway lesions, endobronchial management options are recommended. For distal or parenchymal lesions, external beam radiotherapy (EBRT) is recommended (Grade 1C).

Remark: If these measures are unsuccessful, consideration should be given to bronchial artery embolization to temporize the bleeding. Most reports of bronchial artery embolization are limited by the few cases of lung cancer managed in almost all studies.

Management for Airway-esophageal Fistulas

In patients with tracheoesophageal fistulas (TEFs), double stenting of the esophagus and airway or esophageal stenting is recommended with self-expanding metallic stents (Grade 1B).

Remark: When primary esophageal stenting is to be used, airway compromise must be considered prior to placing the stent. If a concern exists, an airway stent should be placed prior to esophageal stenting.

Management of Malignant Pleural Effusions (MPEs)

Tunneled Pleural Catheter (TPCs) for Palliation

In patients with a symptomatic recurrent MPE with documented re-expandable lung, TPCs or chemical pleurodesis are recommended (Grade 1C).

Remark: In patients with a limited lifespan, serial thoracentesis can be considered.

In patients with a symptomatic recurrent MPE with lung trapping, tunneled catheters are recommended for symptomatic relief and improvement in QOL (Grade 1C).

In lung cancer patients with a suspected MPE in whom the diagnosis of stage IV disease is not confirmed, thoracoscopy is recommended instead of a tunneled catheter due to its diagnostic as well as therapeutic benefit (Grade 1C).

In patients with an MPE, graded talc is the pleural sclerosant that is recommended due to its efficacy and safety profile (Grade 1C).

In lung cancer patients with a malignant effusion, thoracoscopy with talc poudrage is recommended instead of talc slurry through a bedside chest tube for pleurodesis (if there are no contraindications to thoracoscopy) (Grade 1C).

Management of Venous Thromboembolic Disease

See the National Guideline Clearinghouse summary of the American College of Chest Physicians guideline [Prevention of VTE in nonsurgical patients: antithrombotic therapy and prevention of thrombosis, 9th ed: American College of Chest Physicians evidence-based clinical practice guidelines](#).

Management of Depression, Fatigue, Anorexia, and Insomnia

In patients recently diagnosed with lung cancer it is recommended that comprehensive biopsychosocial assessment be performed soon after the diagnosis is made and at key transition points (completion of treatment, disease progression, and new symptom onset) thereafter for the remainder of life (Grade 1C).

In lung cancer patients that identify psychologic and physical symptoms causing distress or interfering with their QOL, it is recommended that these symptoms are addressed by appropriately trained individuals (Grade 1C).

In lung cancer patients with depression, anxiety, excessive daytime sedation and fatigue, medications such as antidepressants, anxiolytics and psychostimulants are recommended to decrease the morbidity associated with these symptoms (Grade 1C).

In lung cancer patients with psychologic symptoms, a comprehensive symptom management plan is recommended. This should include non-pharmacologic interventions integrated with medication management, which may be offered as a single treatment modality (Grade 1C).

In lung cancer patients with insomnia, sedating antidepressants (which target both sleep and mood) are recommended over sedative-hypnotics (which only improve sleep) (Grade 1C).

In lung cancer patients with the subjective experience of breathlessness, interventions specifically designed to manage this symptom using psychologic coping and physical adaptation are recommended (Grade 1C).

Remark: Targeted interventions for breathlessness more effectively decrease distress and improve satisfaction with care than usual care provided during medical follow-up office visits.

In lung cancer patients with psychologic distress, it is suggested that one of several psychologic interventions have demonstrated benefit (including psycho-education, deep breathing, progressive muscle relaxation, guided imagery, cognitive behavioral therapy and supportive psychotherapy) (Grade 2C).

Remark: There is limited evidence to support selection of one intervention over another based on characteristics of the target symptom, patient, or disease status.

Remark: The authors suggest that psychologic interventions to relieve distress are chosen based on patient preference, available skill-set of the health care team, and the available evidence from lung cancer studies.

It is suggested that educational programs responsible for preparing health care professionals to care for persons with cancer should include specific training in psychologic and physical symptom management of symptoms that are frequently associated with cancer diagnosis, treatment and survivorship (Grade 2C).

It is suggested that health care systems providing care to persons with cancer should develop and support integrated programs in psychologic and physical symptom management which are accessible to all (Grade 2C).

Definitions:

Strength of the Recommendations Grading System

Grade of Recommendation	Benefit vs. Risk and Burdens	Methodologic Quality of Supporting Evidence	Implications
Strong recommendation, high-quality	Benefits clearly outweigh risk and burdens or vice versa	Consistent evidence from randomized controlled trials (RCTs) without important limitations or exceptionally	Recommendation can apply to most patients in most circumstances. Further research is very unlikely to change confidence in the estimate of

Grade of Recommendation	Benefit vs. Risk and Burdens	Methodologic Quality of Supporting Evidence	Implications
Strong recommendation, moderate-quality evidence, Grade 1B	Benefits clearly outweigh risk and burdens or vice versa	strong evidence from observational studies Evidence from RCTs with important limitations (inconsistent results, methodologic flaws, indirect or imprecise), or very strong evidence from observational studies	effect Recommendation can apply to most patients in most circumstances. Higher quality research may well have an important impact on confidence in the estimate of effect and may change the estimate
Strong recommendation, low- or very-low-quality evidence, Grade 1C	Benefits clearly outweigh risk and burdens or vice versa	Evidence for at least one critical outcome from observational studies, case series, or from RCTs with serious flaws or indirect evidence	Recommendation can apply to most patients in many circumstances. Higher-quality research is likely to have an important impact on confidence in the estimate of effect and may well change the estimate
Weak recommendation, high-quality evidence, Grade 2A	Benefits closely balanced with risks and burden	Consistent evidence from RCTs without important limitations or exceptionally strong evidence from observational studies	The best action may differ depending on circumstances or patient's or societal values. Further research is very unlikely to change confidence in the estimate of effect
Weak recommendation, moderate-quality evidence, Grade 2B	Benefits closely balanced with risks and burden	Evidence from RCTs with important limitations (inconsistent results, methodologic flaws, indirect or imprecise) or very strong evidence from observational studies	Best action may differ depending on circumstances or patient's or societal values. Higher-quality research may well have an important impact on confidence in the estimate of effect and may change the estimate
Weak recommendation, low- or very-low-quality evidence, Grade 2C	Uncertainty in the estimates of benefits, risks, and burden; benefits, risk, and burden may be closely balanced	Evidence for at least one critical outcome from observational studies, case series, or RCTs, with serious flaws or indirect evidence	Other alternatives may be equally reasonable. Higher-quality research is likely to have an important impact on confidence in the estimate of effect and may well change the estimate

Clinical Algorithm(s)

A pain management algorithm is available in the original guideline document.

Scope

Disease/Condition(s)

Lung cancer

Guideline Category

Management

Treatment

Clinical Specialty

Family Practice

Oncology

Pulmonary Medicine

Intended Users

Advanced Practice Nurses

Allied Health Personnel

Health Care Providers

Nurses

Patients

Physicians

Guideline Objective(s)

- To inform the clinical decisions that must be jointly made by physicians and patients in developing diagnostic, treatment, and management plans so that they can enhance the benefits and reduce the harms associated with various options
- To provide the reader recommendations based on evidence supported by scientific study

Target Population

Patients with lung cancer who develop symptoms related to the disease process or the treatment they are receiving

Interventions and Practices Considered

1. Pain control
 - Thorough assessment of the patient and his or her pain
 - Patient-reported pain scale: visual analog scales (VASs), numerical rating scales (NRSs), verbal rating scales
 - Use of World Health Organization (WHO) analgesic ladder to plan treatment
 - Acetaminophen and/or a non-steroidal anti-inflammatory drug (NSAID) with or without codeine or dihydrocodeine
 - Misoprostol, standard dose proton pump inhibitors, or double-dose histamine H2 antagonists
 - Anticonvulsants (e.g., pregabalin, gabapentin, or carbamazepine)
 - Tricyclic antidepressants (e.g., amitriptyline or imipramine)
 - Oral morphine
 - Oxycodone or hydromorphone
 - Transdermal fentanyl (as an alternative to oral morphine)
 - Methadone
 - Systemic strong opioids
 - Parenteral morphine or transmucosal fentanyl citrate for breakthrough pain
2. Management of airway obstruction
 - Therapeutic bronchoscopy employing mechanical debridement
 - Brachytherapy
 - Tumor ablation
 - Airway stent placement
3. Palliation of cough
 - Evaluation for treatable causes of cough other than cancer
 - Opioids
 - Anti-inflammatory therapy with corticosteroids
4. Palliation of bone metastasis
 - External radiation therapy
 - Bisphosphonates with external beam radiation therapy (EBRT)
 - Surgical fixation (intramedullary nailing)
 - Radiotherapy

- Vertebral augmentation procedures
5. Palliation of brain metastasis
 - Dexamethasone
 - Surgical resection
 - Stereotactic radiosurgery (SRS)
 - Whole brain radiation
 6. Palliation of spinal cord compression
 - Magnetic resonance imaging (MRI)
 - High-dose dexamethasone and radiotherapy
 - Neurosurgical consultation
 - Surgery followed by radiation therapy
 7. Palliation of superior vena cava (SVC) obstruction
 - Definitive diagnosis by histologic or cytologic methods
 - Chemotherapy
 - Radiation therapy and/or stent insertion, with consideration of necessary anticoagulation for stents
 - Vascular stents
 8. Management of hemoptysis
 - Securing the airway with a single-lumen endotracheal tube
 - Bronchoscopy
 - Endobronchial management options (argon plasma coagulation, neodymium-doped:yttrium aluminum garnet [Nd:YAG] laser, electrocautery)
 - EBRT
 - Bronchial artery embolization to temporize the bleeding
 9. Management for airway-esophageal fistulas: double stenting of the esophagus and airway or esophageal stenting with self-expanding metallic stents
 10. Management of malignant pleural effusions (MPEs)
 - Tunneled pleural catheter (TPC)
 - Chemical pleurodesis
 - Serial thoracentesis
 - Thoracoscopy (with or without talc poudrage)
 - Graded talc
 11. Management of venous thromboembolic disease
 12. Management of depression, fatigue, anorexia, and insomnia
 - Comprehensive biopsychosocial assessment
 - Antidepressants, anxiolytics and psychostimulants
 - Comprehensive symptom management plan
 - Non-pharmacologic interventions integrated with medication management
 - Psychologic coping and physical adaptation
 - Psychologic interventions including psycho-education, deep breathing, progressive muscle relaxation, guided imagery, cognitive behavioral therapy, and supportive psychotherapy

Note: The following were considered but not recommended for pain control: ketamine, lidocaine 5% plasters, cannabinoids, and transdermal fentanyl (as first-line use).

Major Outcomes Considered

- Ability to walk
- Continence (days)
- Length of response (days)
- Overall survival (days)
- Rate of pleurodesis
- Quality of life (QOL)

Methodology

Methods Used to Collect/Select the Evidence

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

To consistently format the searches, the panel used the population, intervention, comparator, outcome (PICO) format. The list of questions generated previous to each search can be seen in Table S1 in the supporting data (see the "Availability of Companion Documents" field).

The writing team searched Ovid MEDLINE, Google Scholar, CINAHL, PsycINFO, Cochrane, EMBASE, Web of Science, and review of references. Searches extended back more than 10 years in all reviews. Upon completion of the searches, the panel first performed a title review of those materials. This was followed by an abstract review, and then articles were selected for full text review by one of the article authors. MeSH terms and key words were searched with no limiters of language or article type, as the panel suspected many of the data were observational. Data were then abstracted and the text and recommendations written.

Number of Source Documents

Not stated

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Not Given)

Rating Scheme for the Strength of the Evidence

Not stated

Methods Used to Analyze the Evidence

Review of Published Meta-Analyses

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

Assessment of Study Quality

Systematic reviews and meta-analyses were assessed using Documentation and Appraisal Review Tool (DART) (R. L. Diekemper; B. K. Ireland, MD; and L. R. Merz, PhD, MPH, DART, unpublished data, 2012), which was developed as an improved alternative to the existing tools for use in a clinical setting. However, this tool has been adopted for use in American College of Chest Physicians (ACCP) guidelines and consensus statements since 2011.

Quality was assessed for each study as well as for the body of relevant evidence. Based on the population, intervention, comparator, and outcome (PICO) questions and volume of available literature, multiple study designs were included in the systematic reviews of the literature. Randomized controlled trials (RCTs) primarily indicate benefits, but whenever observational studies met inclusion criteria they were often helpful in identifying harms. Observational studies were also examined when RCTs were not available to answer a particular PICO question. Allowing for multiple study designs resulted in the need for multiple quality assessment tools. Tools were chosen for assessing RCTs, observational studies, and diagnostic studies. The quality assessment tool for RCTs (R. L. Diekemper, B. K. Ireland, and L. R. Merz, unpublished data, 2012) was used for assessing the quality of RCTs, and a tool developed by the committee of the ninth edition of the Antithrombotics Guidelines was used for assessing the quality of observational studies. Diagnostic studies were assessed using the Quality Assessment Tool for Diagnostic Accuracy Studies (QUADAS).

Meta-analyses

If a recently published good-quality meta-analysis was available, then it was used to inform the recommendations. When a good-quality meta-analysis was not available, guideline authors were encouraged to perform their own meta-analyses. Meta-analyses were performed when the data were fairly homogeneous. If a study was deemed poor quality, then it was not included in the pooled analysis. Heterogeneity of the pooled results was assessed using a χ^2 test and Higgins I^2 , and a forest plot was examined for consistency of the results. The random effects model was chosen a priori as the appropriate model for pooling the data because it accounts for heterogeneity among the included studies. Results from the meta-analyses are available in the supplementary materials that can be downloaded from the Journal website under the corresponding article in the table of contents.

Methods Used to Formulate the Recommendations

Expert Consensus

Informal Consensus

Description of Methods Used to Formulate the Recommendations

Panel Composition and Responsibilities

A call for applications to serve on the 3rd edition of the American College of Chest Physicians (ACCP) Lung Cancer Guidelines (LC III) panel was put forth to the ACCP membership, to past panelists, and to other organizations that have previously endorsed earlier editions of these guidelines or appointed representatives to serve on those panels. Guiding the team was the LC III Executive Committee, composed of a Panel Chair, Vice Chair, Liaison to the Guidelines Oversight Committee (GOC), and two staff members, one serving as an adviser and the other as the lead methodologist. The GOC appointed the Liaison and the Chair, who was required to be free of conflicts of interest (COI). This Executive Committee provided general oversight and guidance; multiple reviews of research questions, article outlines, manuscripts, evidence tables, and other supporting documents; and facilitation of the final conference discussions and voting. As the scope was defined, content experts in each major area were identified to serve as topic editors and nominated by the Panel Chair to be advanced to the GOC for the requisite qualifications and COI review and approval process. These topic editors organized their research and writing teams, oversaw the work of the individual members, edited separate contributions into synthesized manuscripts, presented evidence at the final conference, and managed any of their committee members who were approved with management stipulations relevant to their COIs.

Each topic editor was initially charged with proposing individuals to support their topic committees with expertise in the content area and/or methodology. With the Chair's approval, these individuals were nominated for GOC reviews for COI and expertise. In some cases, GOC staff helped to locate additional methodologic support when it was determined to be necessary for various article committees. This resulted in an international panel of >100 multidisciplinary experts across 24 articles representing the fields of pulmonary medicine, critical care medicine, thoracic surgery, medical and radiation oncology, pathology, integrative medicine, primary care, health-care research, guidelines methodology, and epidemiology. Nineteen international organizations that are also dedicated to advancing research and practice in the area of lung cancer were invited to appoint representatives to this guideline project as adjunct participants. These individuals, unless already approved panelists, were not considered full voting members of the panel, since they had not been through the same ACCP COI review, but were included at the final conference, participated fully in the discussions, and provided external review and feedback on the manuscripts and supporting documentation.

Formulating the Recommendations

In most cases the topic editors, along with the other completely non-conflicted members of the article committee, formulated the recommendations. The summarized evidence tables and profiles (where profiles existed) provided the foundation for the recommendations. In formulating the recommendations, panelists considered not only the body of evidence but also the balance between the benefits and harms and considerations of other factors, such as cost or resource availability considerations and patient values and preferences, which might vary widely for some recommendations. These additional considerations are described in a Remarks section, which appears just below the relevant recommendation in the publication, each time the recommendation appears.

Grading the Recommendations

Recommendations that are strong must be differentiated from those that are weak or weaker. Thus, the ACCP Grading System was used (see the "Rating Scheme for the Strength of the Recommendations" field), and the wording of the recommendations is explicit. This grading system has been used since 2005 and is based on two dimensions: the balance of benefits to harms and the quality of the evidence base. If the benefits clearly outweigh the harms or the harms clearly outweigh the benefits, the strength of the recommendation is considered strong and graded as a 1. In most

cases, when there is strong confidence that the benefits outweigh the harms, most patients would choose the intervention endorsed in that recommendation. However, when the tradeoffs between desirable and undesirable consequences are not as clear, variability in patient preferences and values often becomes germane to the decision-making conversation.

Weak recommendations are those for which the benefits and harms are more equally balanced, and thus a clear choice is not as obvious; these are graded with a 2. Strong recommendations are phrased, "the panel recommends," whereas weak recommendations are phrased "the panel suggests." Accompanying these indications of the strength of a recommendation is a letter score (A, B, or C) representing the grading of the body of relevant literature.

In grading the quality of the evidence, RCTs start with a high score but might be downgraded to moderate or even low based on the following criteria: limitations in the study design or conduct of the trial, imprecision, indirectness relative to the specifics of the PICO question, inconsistency in the results, and risk of reporting bias. Observational studies, on the other hand, start off as low-level evidence but can be upgraded to moderate or even high if exceptionally large and consistent treatment effects increase confidence in the findings, especially if there is a strong dose-response gradient.

The final grades are combinations reflecting the strength of the recommendation and the quality of the evidence. Strong recommendations with high quality evidence, grade of 1A, are less common than in past editions of these guidelines, since the evidence is assessed with greater rigor for most topics, and few studies without important limitations are available.

However, recommendations that do attain this score are those for which the panel could state with confidence that new studies would be unlikely to change the direction of the effect. These recommendations apply to most patients in most circumstances. But as the grades decline, patient values and preferences likely would play an increasingly greater role in determining the best treatments or interventions for each patient.

The Final Conference

As the evidence reviews were completed and the tables and profiles prepared, the manuscripts and recommendations were drafted. Members of the article committees convened by phone or e-mail to discuss the evidence and work on drafting and grading the recommendations. These discussions generally resulted in agreement on both the quality of the evidence and strength of the recommendations.

The manuscripts and supporting tables were then reviewed by members of the Executive Committee and, after several iterations, the revised versions were shared among all panelists and the representatives of invited organizations in advance of the conference. The other panelists and representatives were asked not only to provide feedback but also to review the recommendations to identify any controversies. A recommendation was deemed to be controversial if at least one person disagreed with the wording or the grading, if there was controversy in practice, if there were wide variations in practice, or if at least one person asked that it be discussed among the broader panel and association representatives. These identified controversies composed the main agenda for the conference.

See the "Methodology for Development of Guidelines for Lung Cancer" (see the "Availability of Companion Documents" field) for more information.

Rating Scheme for the Strength of the Recommendations

Strength of the Recommendations Grading System

Grade of Recommendation	Benefit vs. Risk and Burdens	Methodologic Quality of Supporting Evidence	Implications
Strong recommendation, high-quality evidence, Grade 1A	Benefits clearly outweigh risk and burdens or vice versa	Consistent evidence from randomized controlled trials (RCTs) without important limitations or exceptionally strong evidence from observational studies	Recommendation can apply to most patients in most circumstances. Further research is very unlikely to change confidence in the estimate of effect
Strong recommendation, moderate-quality evidence, Grade 1B	Benefits clearly outweigh risk and burdens or vice versa	Evidence from RCTs with important limitations (inconsistent results, methodologic flaws, indirect or imprecise), or very strong evidence from observational studies	Recommendation can apply to most patients in most circumstances. Higher quality research may well have an important impact on confidence in the estimate of effect and may change the estimate
Strong recommendation,	Benefits clearly outweigh risk and burdens or vice	Evidence for at least one critical outcome from observational studies,	Recommendation can apply to most patients in many circumstances. Higher-quality research is

Grade of Recommendation	Benefit vs. Risk and Burdens	Methodologic Quality of Supporting Evidence	Implications
low- or very-low-quality evidence, Grade 1C	versus	case series, or from RCTs with serious flaws or indirect evidence	likely to have an important impact on confidence in the estimate of effect and may well change the estimate
Weak recommendation, high-quality evidence, Grade 2A	Benefits closely balanced with risks and burden	Consistent evidence from RCTs without important limitations or exceptionally strong evidence from observational studies	The best action may differ depending on circumstances or patient's or societal values. Further research is very unlikely to change confidence in the estimate of effect
Weak recommendation, moderate-quality evidence, Grade 2B	Benefits closely balanced with risks and burden	Evidence from RCTs with important limitations (inconsistent results, methodologic flaws, indirect or imprecise) or very strong evidence from observational studies	Best action may differ depending on circumstances or patient's or societal values. Higher-quality research may well have an important impact on confidence in the estimate of effect and may change the estimate
Weak recommendation, low- or very-low-quality evidence, Grade 2C	Uncertainty in the estimates of benefits, risks, and burden; benefits, risk, and burden may be closely balanced	Evidence for at least one critical outcome from observational studies, case series, or RCTs, with serious flaws or indirect evidence	Other alternatives may be equally reasonable. Higher-quality research is likely to have an important impact on confidence in the estimate of effect and may well change the estimate

Cost Analysis

In a subsequent analysis of the Radiation Therapy Oncology Group (RTOG) 97-14 trial, a Markov model was used to evaluate the cost-effectiveness of 30 Gy in 10 fractions compared with 8 Gy in one fraction. The expected mean cost and quality-adjusted survival in months for patients receiving 8 Gy in one fraction and 30 Gy in 10 fractions was \$998 and 7.2 months and \$2,316 and 9.5 months, respectively. The incremental cost-effectiveness ratio was \$6,973/quality-adjusted life year.

Method of Guideline Validation

External Peer Review

Internal Peer Review

Description of Method of Guideline Validation

Internal and External Peer Review

Once Executive Committee approval was received, the articles were submitted to American College of Chest Physicians (ACCP) staff for several layers of review. All reviewers were required to undergo a full conflict of interest (COI) appraisal before being approved. In the first round of reviews, the Thoracic Oncology NetWork reviewed the content of the manuscripts and the members of the Guidelines Oversight Committee (GOC) assessed the manuscripts for adherence to the methodology and conformance with the evidence. The ACCP President also appointed members of the Board of Regents to evaluate the guidelines in depth. All comments were collated into spreadsheets to ensure that they were appropriately answered. GOC and board reviewers discussed each comment and determined which should be mandatory for the authors to amend and which were provided as suggestions for improvement. All reviews and comments were anonymous, and authors were required to respond to all mandatory issues either by revising the manuscripts or providing written justification explaining why they did not agree with the reviewers' comments.

The revised manuscripts were submitted for round II review, simultaneously with the Journal peer review. Once the GOC and board reviewers approved the manuscripts, the ACCP President, President Elect, President Elect Designee, and Immediate Past President reviewed the guidelines. Approval was granted pending confirmation from the Board of Regents, before submission to the journal for final review by the Journal Editor. In addition to this extensive review process, which included nearly 30 individual reviewers from the ACCP leadership, external organizations were provided with opportunities to provide feedback before, during, and just after the conference. This final version was submitted for consideration for endorsement to all of the invited organizations, whether or not they sent representatives to the conference. However, once the guidelines were approved by the ACCP Board of Regents, no further changes were accepted. Organizations that provided endorsements are listed in each article.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of supporting evidence is identified and graded for each recommendation (see the "Major Recommendations" field).

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Appropriate symptom management in patients with lung cancer

Potential Harms

- The principal side effects of opioid use are constipation, nausea/vomiting, and drowsiness. Of these, constipation is the only side effect to which tolerance does not usually develop. Caution should be exercised in prescribing graduated doses of these drugs because of the risk of respiratory depression and hypoventilation. Renal impairment increases the possibility of opioid toxicity.
- The primary difficulty with corticosteroids is the side effects that patients experience (cushingoid facies, peripheral edema, gastrointestinal [GI] bleeding, psychosis, and steroid-induced myopathy, among others). Therefore, patients should only be on corticosteroids if they are symptomatic.
- In one study, the toxicity profile was found to be significant: 29% side effects, 14% serious (one fatal ulcer, one rectal bleeding, one GI perforation, one sigmoid perforation) with high-dose dexamethasone therapy.
- In one study, the rate of complications of multimodality therapeutic bronchoscopy ranged from 3% to 8%, with one mortality related to asphyxiation due to an obstructed stent at 30 days postprocedure.
- Side effects of radiation therapy

Contraindications

Contraindications

Contraindications to surgical treatment of metastatic disease to long bones include a survival expectancy <4 weeks and a poor general condition that is an obstacle to a safe operation.

Qualifying Statements

Qualifying Statements

- American College of Chest Physicians (ACCP) guidelines are intended for general information only, are not medical advice, and do not replace professional medical care and physician advice, which always should be sought for any medical condition. The complete disclaimer for this guideline can be accessed at the [CHEST Web site](#) .
- Although the ACCP is moving toward the production of evidence profiles for all guideline recommendations, there were many recommendations for which profiles were not developed, mostly because of resource constraints. When possible, methodologists created evidence profiles, and all panelists were educated on how to read and interpret them. The population, intervention, comparator, and outcome (PICO)-based systematic literature review process was followed for most recommendations, but there were some that could have benefited from meta-analyses.
- One limitation of all guidelines today is that they are not able to adequately address complex patients with multiple morbidities. This is largely because these patients are generally excluded from clinical trials and are often not included in observational studies. Since guidelines are

reliant on evidence published in the peer-reviewed literature, the scientific foundation impedes the process of providing good guidance for these patients and is a limitation in these guidelines. Therefore, the ACCP encourages funding agencies to ensure that topics with limited evidence are addressed in future research.

Implementation of the Guideline

Description of Implementation Strategy

Dissemination and Implementation

These guidelines are widely disseminated through the *CHEST* journal publication, National Guideline Clearinghouse, and Guidelines International Network library. Additional clinical resources will soon be available to users of CHEST Evidence, an upcoming tool for searching the content of American College of Chest Physicians (ACCP) guidelines.

As the expanding research into diagnostic techniques and treatment options continues to evolve, the guidelines must be updated and kept current. This edition of the ACCP Lung Cancer Guidelines will be the last to be published as a complete collection, as the ACCP is now embarking on a new living guidelines model (LGM) for revising existing recommendations and developing new recommendations as the literature evolves. This will include a continual assessment of the currency of these recommendations relevant to new research studies as they are published. The review cycle for the ACCP Lung Cancer Guidelines will begin 1 year after publication unless the content experts who monitor the literature bring a recommendation or set of related recommendations to the attention of the Guideline oversight Committee (GOC), suggesting that those recommendations are in need of updating sooner. The new LGM will permit a more nimble approach to guideline development but also requires a point-of-care accessible vehicle, CHEST Evidence, for the users to readily search for the most current version. These features will be described in greater detail in upcoming publications. As a step in this direction, these guidelines will be published primarily online with a printed version of the Executive Summary, containing all of the recommendations, the introduction, and this article on methodology. All narratives for each article with their supporting tables, figures, and algorithms will be available online at journal.publications.chestnet.org .

Implementation Tools

Clinical Algorithm

Mobile Device Resources

Patient Resources

Quick Reference Guides/Physician Guides

Resources

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Getting Better

Living with Illness

IOM Domain

Effectiveness

Identifying Information and Availability

Bibliographic Source(s)

Simoff MJ, Lally B, Slade MG, Goldberg WG, Lee P, Michaud GC, Wahidi MM, Chawla M. Symptom management in patients with lung cancer: diagnosis and management of lung cancer, 3rd ed: American College of Chest Physicians evidence-based clinical practice guidelines. Chest. 2013 May;143(5 Suppl):e455S-97S. [295 references] [PubMed](#)

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2003 Jan (revised 2013 May)

Guideline Developer(s)

American College of Chest Physicians - Medical Specialty Society

Source(s) of Funding

- The development of this guideline was supported primarily by the American College of Chest Physicians (ACCP). The lung cancer guidelines conference was supported in part by a grant from the Lung Cancer Research Foundation. The publication and dissemination of the guidelines was supported in part by a 2009 independent educational grant from Boehringer Ingelheim Pharmaceuticals, Inc.
- Role of sponsors: The ACCP was solely responsible for the development of these guidelines. The remaining supporters played no role in the development process. External supporting organizations cannot recommend panelists or topics, nor are they allowed prepublication access to the manuscripts and recommendations. Further details on the Conflict of Interest (COI) Policy are available online at <http://chestnet.org> .
- See the methodology companion (see the "Availability of Companion Documents" field) for a complete discussion of the source of funding for this guideline.

Guideline Committee

American College of Chest Physicians (ACCP) Expert Panel on Lung Cancer Guidelines

Composition of Group That Authored the Guideline

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Financial Disclosures/Conflicts of Interest

- Conflicts of Interest (COI) grids reflecting the conflicts of interest that were current as of the date of the conference and voting are posted in the online supplementary materials.
- Financial/nonfinancial disclosures: The authors have reported to *CHEST* the following conflicts of interest: Ms Goldberg owns some share in

pharmaceutical or laboratory tests and services companies. However, these portfolios are managed by financial advisors. Dr Wahidi has received educational grants and served as a consultant with Pinnacle Biologics Inc. Drs Simoff, Lally, Slade, Lee, Michaud, Wahidi, and Chawla have reported that no potential conflicts of interest exist with any companies/organizations whose products or services may be discussed in this article.

- See the methodology companion (see the "Availability of Companion Documents" field) for a complete discussion of the conflict of interest procedures and requirements for the guideline panel.

Guideline Endorser(s)

American Association for Bronchology and Interventional Pulmonology - Medical Specialty Society

European Society of Thoracic Surgeons - Professional Association

Oncology Nursing Society - Professional Association

Society of Thoracic Surgeons - Medical Specialty Society

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: Kvale PA, Selecky PA, Prakash UB, American College of Chest Physicians. Palliative care in lung cancer: ACCP evidence-based clinical practice guidelines (2nd edition). Chest. 2007 Sep;132(3 Suppl):368S-403S.

Guideline Availability

Electronic copies: Available to subscribers of [Chest - The Cardiopulmonary and Critical Care Journal](#) . Also available to Chest subscribers through the [Chest app](#) for iPhone and iPad.

Print copies: Available from the American College of Chest Physicians, Products and Registration Division, 3300 Dundee Road, Northbrook IL 60062-2348.

Availability of Companion Documents

The following are available:

- Symptom management in patients with lung cancer: diagnosis and management of lung cancer, 3rd ed: American College of Chest Physicians evidence-based clinical practice guidelines. Supporting data. Electronic copies: Available to subscribers of [Chest - The Cardiopulmonary and Critical Care Journal](#) .
- Detterbeck FC, Zelman Lewis S, Diekemper R, Addrizzo-Harris D, Alberts MW. Diagnosis and management of lung cancer, 3rd ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Executive summary. Chest 2013 May;143(5 Suppl):7S-37S. Electronic copies: Available from the [Chest - The Cardiopulmonary and Critical Care Journal Web site](#) .
- Alberts WM. Introduction to the third edition: diagnosis and management of lung cancer, 3rd ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest 2013 May;143(5 Suppl):38S-40S. Electronic copies: Available from the [Chest - The Cardiopulmonary and Critical Care Journal Web site](#) .
- Zelman Lewis S, Diekemper R, Addrizzo-Harris DJ. Methodology for development of guidelines for lung cancer: diagnosis and management of lung cancer, 3rd ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest 2013 May;143(5 Suppl):41S-e50S. Electronic copies: Available from the [Chest - The Cardiopulmonary and Critical Care Journal Web site](#) .
- Alberg AJ, Brock MV, Ford JG, Samet JM, Spivack SD. Epidemiology of lung cancer: diagnosis and management of lung cancer, 3rd ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest 2013 May;143(5 Suppl):e1S-e29S. Electronic copies: Available to subscribers of [Chest - The Cardiopulmonary and Critical Care Journal](#) .

- Nana-Sinkham SP, Powell CA. Molecular biology of lung cancer: diagnosis and management of lung cancer, 3rd ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest 2013 May;143(5 Suppl):e30S-e39S. Electronic copies: Available to subscribers of [Chest - The Cardiopulmonary and Critical Care Journal](#) .

Print copies: Available from the American College of Chest Physicians, Products and Registration Division, 3300 Dundee Road, Northbrook IL 60062-2348.

The following is also available:

- Highlights of the ACCP diagnosis and management of lung cancer guidelines, 3rd ed. Podcast. Available from the [Chest - The Cardiopulmonary and Critical Care Journal Web site](#) .

Patient Resources

The following is available:

- Lung cancer: understanding the diagnosis. Northbrook (IL): American College of Chest Physicians; 2010. 7 p. Electronic copies: Available in Portable Document Format (PDF) from the [OneBreath.org Web site](#) .

Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By providing access to this patient information, it is not the intention of NGC to provide specific medical advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline's content.

NGC Status

This NGC summary was completed by ECRI on September 3, 2003. The information was verified by the guideline developer on October 1, 2003. This summary was updated on May 3, 2005 following the withdrawal of Bextra (valdecoxib) from the market and the release of heightened warnings for Celebrex (celecoxib) and other nonselective nonsteroidal anti-inflammatory drugs (NSAIDs). This summary was updated by ECRI on June 16, 2005, following the U.S. Food and Drug Administration advisory on COX-2 selective and non-selective non-steroidal anti-inflammatory drugs (NSAIDs). This NGC summary was updated by ECRI Institute on November 29, 2007. The updated information was verified by the guideline developer on December 21, 2007. This summary was updated by ECRI Institute on May 1, 2009 following the U.S. Food and Drug Administration advisory on antiepileptic drugs. This summary was updated by ECRI Institute on March 16, 2011 following the U.S. Food and Drug Administration advisory on acetaminophen-containing prescription products. This summary was updated by ECRI Institute on August 21, 2013. This summary was updated by ECRI Institute on July 3, 2014 following the U.S. Food and Drug Administration advisory on Epidural Corticosteroid Injection. This summary was updated by ECRI Institute on September 18, 2015 following the U.S. Food and Drug Administration advisory on non-aspirin nonsteroidal anti-inflammatory drugs (NSAIDs). This summary was updated by ECRI Institute on June 2, 2016 following the U.S. Food and Drug Administration advisory on Opioid pain medicines. This summary was updated by ECRI Institute on October 21, 2016 following the U.S. Food and Drug Administration advisory on opioid pain and cough medicines combined with benzodiazepines.

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